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(71) Applicant (for all designated States except US): ASTRA AKTIEBOLAG [SE/SE]; S-151 85 Södertälje (SE).				
(72) Inventors; and				
(75) Inventors/Applicants (for US only): SMITH, Douglas [US/US]; 2 Mayflower Lane, Gloucester, MA 01930 (US). ALM, Richard, A. [AU/US]; 28 Russet Hill Road, Ashland, MA 01721 (US).				
(74) Agents: MANDRAGOURAS, Amy, E. et al.; Lahive & Cockfiel, LLP, 28 State Street, Boston, MA 02109 (US).				

(54) Title: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO *HELICOBACTER PYLORI* AND VACCINE COMPOSITIONS THEREOF

## (57) Abstract

Recombinant or substantially pure preparations of *H. pylori* polypeptides are described. The nucleic acids encoding the polypeptides also are described. The *H. pylori* polypeptides are useful for diagnostics and vaccine compositions.

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CLAIMS

1. An isolated nucleic acid comprising a nucleotide sequence encoding an  
5 *H. pylori* polypeptide at least about 60% homologous to an amino acid sequence  
selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
2. An isolated nucleic acid comprising a nucleotide sequence encoding an  
10 *H. pylori* polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID  
NO: 146.
3. An isolated nucleic acid which encodes an *H. pylori* polypeptide,  
comprising a nucleotide sequence at least about 60% homologous to a nucleotide  
15 sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a  
complement thereof.
4. The isolated nucleic acid of claim 1, comprising a nucleotide sequence  
selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement  
20 thereof.
5. An isolated nucleic acid molecule encoding an *H. pylori* polypeptide,  
comprising a nucleotide sequence which hybridizes under stringent hybridization  
conditions to a nucleic acid molecule comprising the nucleotide sequence selected from  
the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.  
25
6. An isolated nucleic acid comprising a nucleotide sequence of at least 8  
nucleotides in length, wherein the sequence hybridizes under stringent hybridization  
conditions to a nucleic acid having a nucleotide sequence selected from the group  
consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.  
30
7. An isolated nucleic acid comprising a nucleotide sequence encoding an  
*H. pylori* cell envelope polypeptide or a fragment thereof, said nucleic acid selected  
from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID  
NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID  
35 NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID  
NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID  
NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID

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NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21, or a complement thereof.

8. The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48, or a complement thereof.

9. The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71, or a complement thereof.

10. The isolated nucleic acid of claim 9, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO: 71, or a complement thereof.

11. The isolated nucleic acid of claim 9, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, or a complement thereof.

12. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:

101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

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13. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

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14. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

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15. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO: 144.

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16. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.

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17. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ

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5 ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68, or a complement thereof.

10 18. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.

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19. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73, or a complement thereof.

20. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.

21. A probe comprising a nucleotide sequence consisting of at least 8 nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.

22. A recombinant expression vector comprising the nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19 or 20 operably linked to a transcription regulatory element.

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23. A cell comprising a recombinant expression vector of claim 22.

24. A method for producing an *H. pylori* polypeptide comprising culturing a cell of claim 23 under conditions that permit expression of the polypeptide.

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25. The method of claim 24, further comprising purifying the polypeptide from the cell.

26. A method for detecting the presence of a *Helicobacter* nucleic acid in a sample comprising:

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(a) contacting a sample with a nucleic acid of any of claims 6 or 21 so that a hybrid can form between the probe and a *Helicobacter* nucleic acid in the sample; and

(b) detecting the hybrid formed in step (a), wherein detection of a hybrid indicates the presence of a *Helicobacter* nucleic acid in the sample.

15

27. An isolated *H. pylori* polypeptide comprising an amino acid sequence at least about 60% homologous to an *H. pylori* polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.

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28. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.

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29. The isolated *H. pylori* polypeptide of claim 28, wherein said polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.

30. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.

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31. An isolated *H. pylori* polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.

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32. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ

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ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

33. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

34. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

35. The isolated polypeptide of claim 34, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO: 144.

36. The isolated polypeptide of claim 34, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.



37. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

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38. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

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39. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

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40. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO: 71.

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41. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58.

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42. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.

43. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.

44. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.

45. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.

46. A fusion protein comprising an *H. pylori* polypeptide which comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 operatively linked to a non-*H. pylori* polypeptide.

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47. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one isolated nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19, or 20.

5 48. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one *H. pylori* polypeptide or a fragment thereof of any of claims 26, 27, 28, 29, 30, 31, 32, 37, 42, 43, 44 or 45.

10 49. A vaccine formulation of claim 47, further comprising a pharmaceutically acceptable carrier.

50. A vaccine formulation of claim 48, further comprising a pharmaceutically acceptable carrier.

15 51. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises an adjuvant.

20 52. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises an adjuvant.

53. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises a delivery system.

25 54. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises a delivery system.

55. A vaccine formulation of claim 53, wherein the delivery system comprises a live vector.

30 56. A vaccine formulation of claim 54, wherein the delivery system comprises a live vector.

35 57. A vaccine formulation of claim 55, wherein the live vector is a bacteria or a virus.

58. A vaccine formulation of claim 56, wherein the live vector is a bacteria or a virus.

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59. A vaccine formulation of claim 53, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.

5 60. A vaccine formulation of claim 54, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.

61. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 47, such that  
10 treatment or reduction of risk of *H. pylori* infection occurs.

62. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 48, such that treatment or reduction of risk of *H. pylori* infection occurs.  
15

63. A method of producing a vaccine formulation comprising: combining at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.  
20

64. A method of producing a vaccine formulation comprising:  
(a) providing at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146; and  
(b) combining at least one said isolated *H. pylori* polypeptide or a  
25 fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.

65. A method of producing a vaccine formulation comprising:  
(a) culturing a cell under condition that permit expression of an *H.*  
30 *pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146;  
(b) isolating said *H. pylori* polypeptide from said cell; and  
(c) combining at least one said isolated *H. pylori* polypeptide or a  
fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine  
35 formulation.

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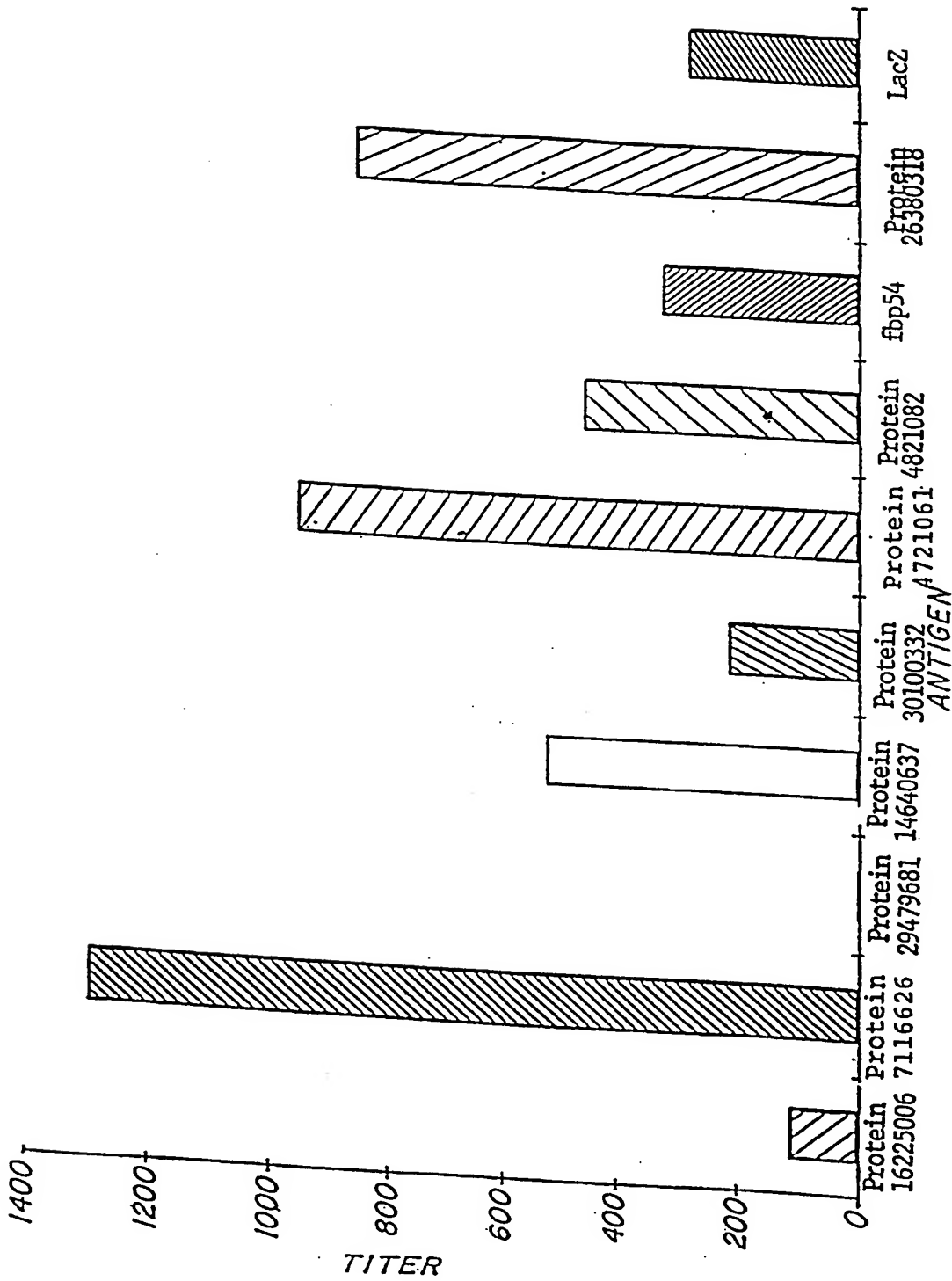


FIG. 1

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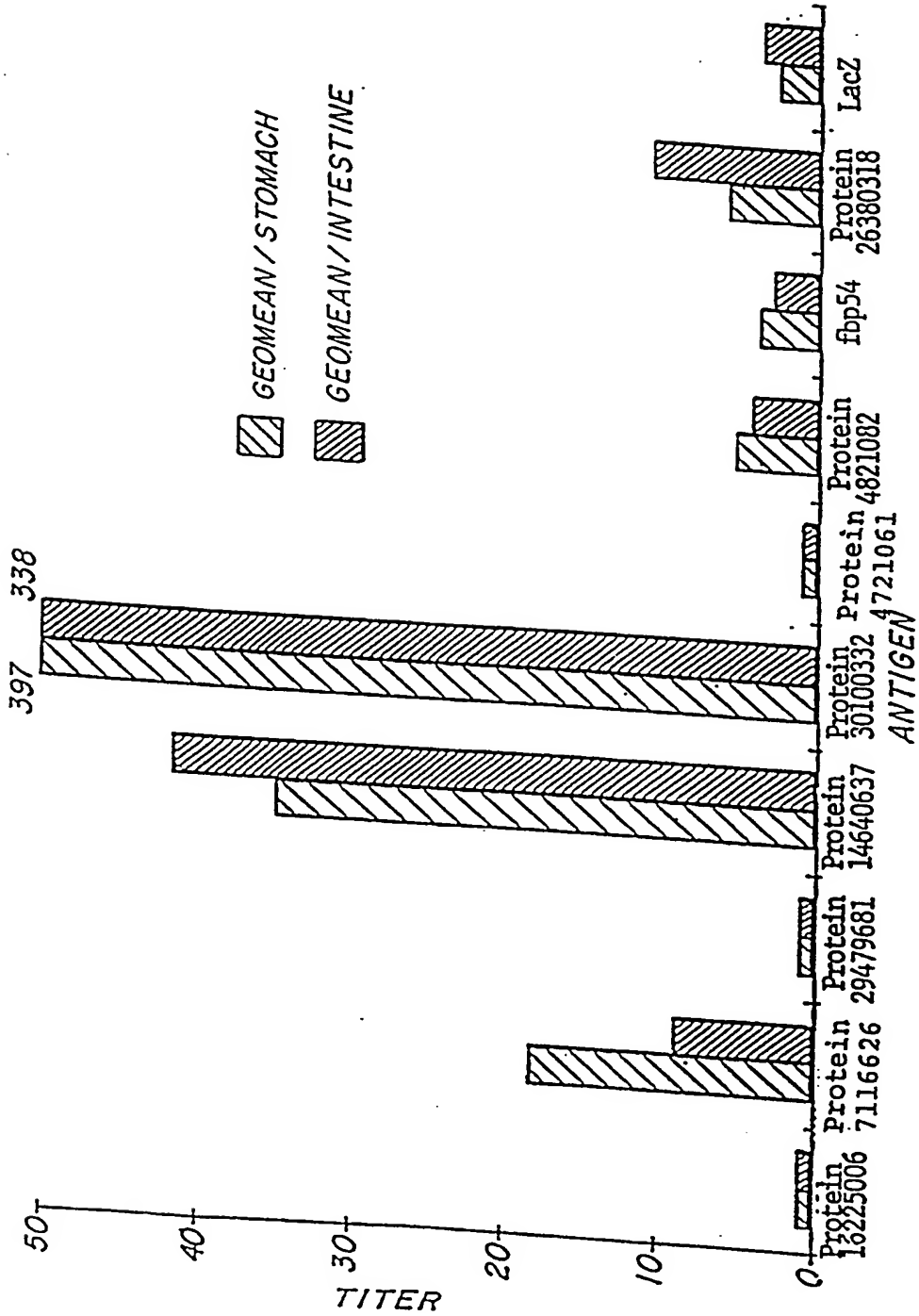


FIG. 2

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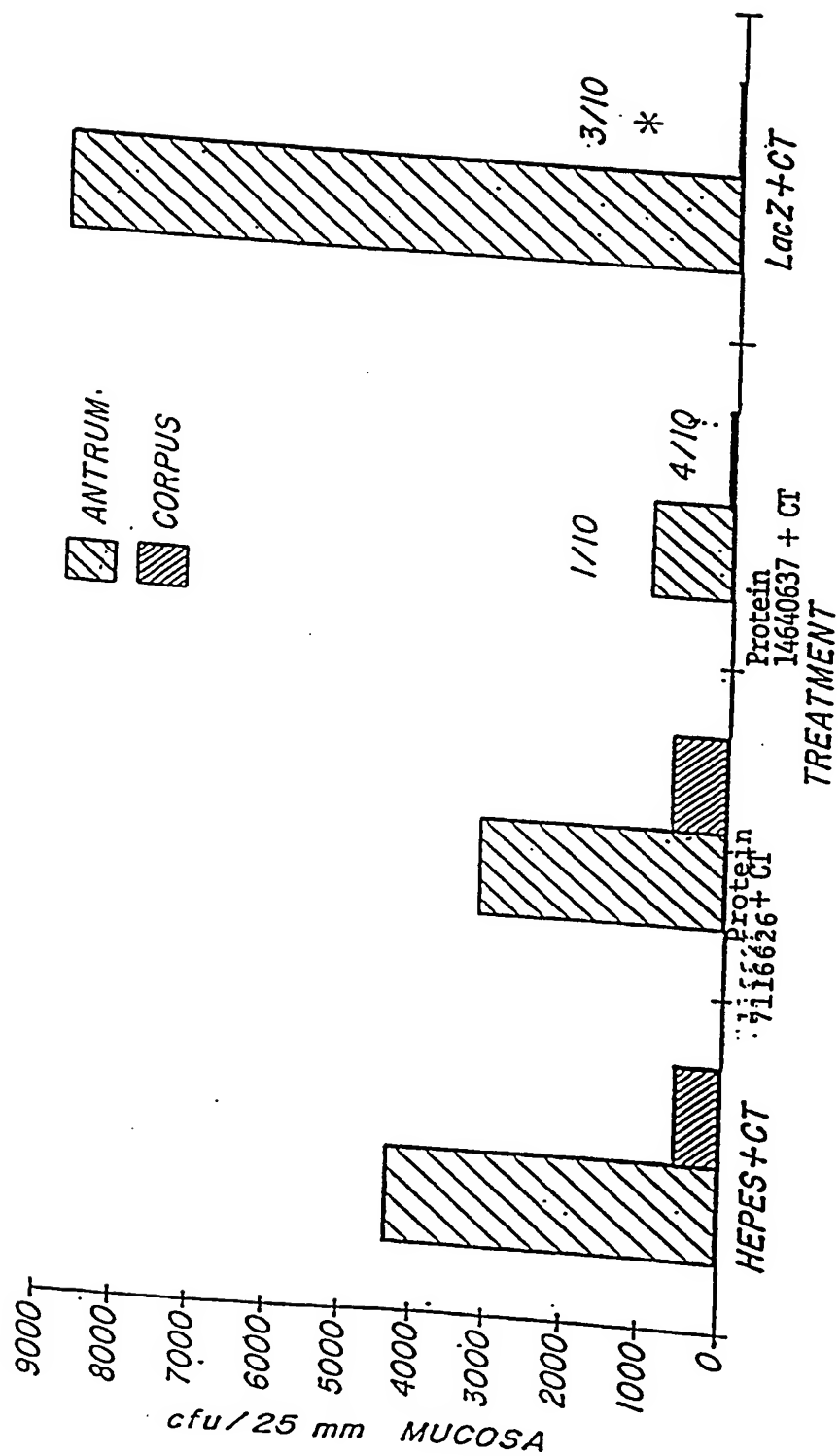


FIG. 3

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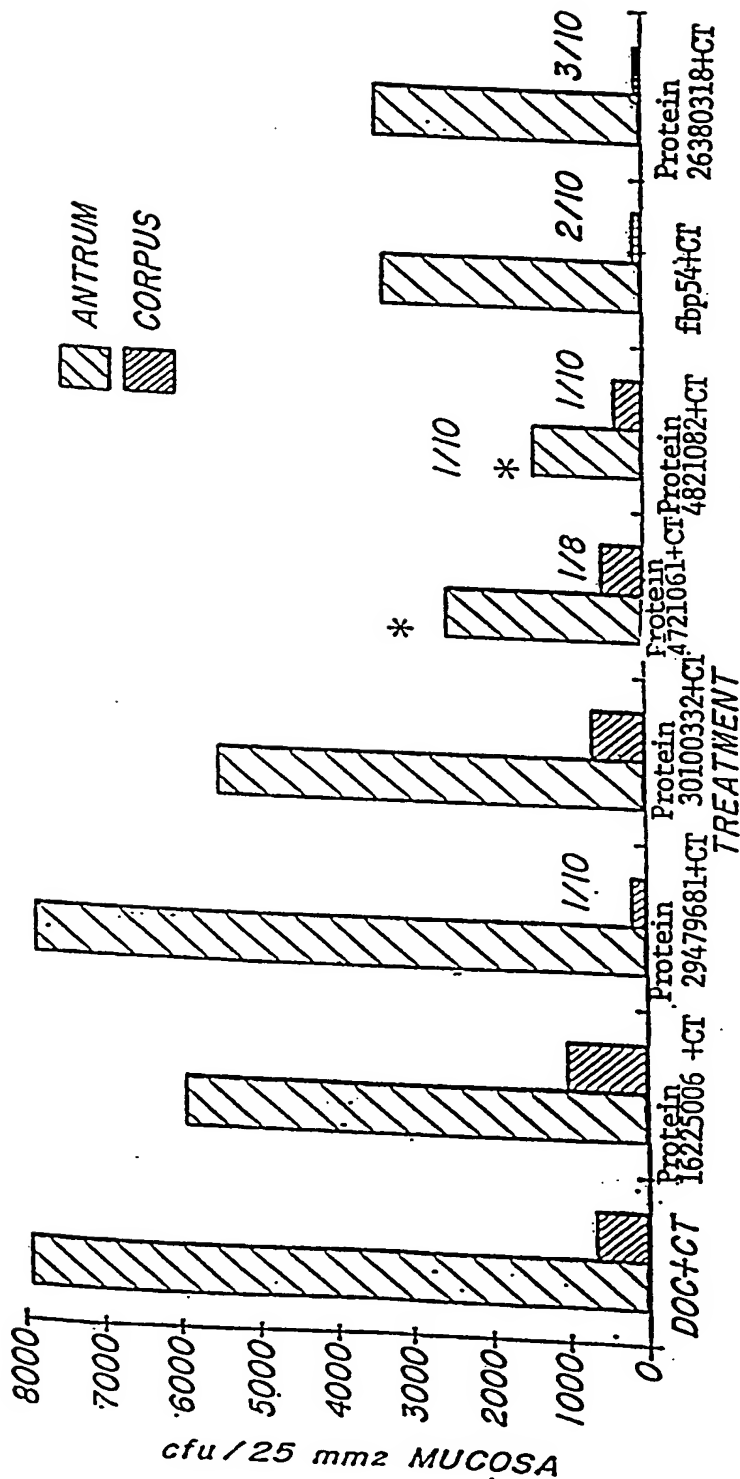


FIG. 4

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aa SeqID#

74 -----MIKRIAC-ILSLSASLALAGEVNBLOCK A  
115 -----MIKRIAC-ILSLSASLALAGEVNGFFMGAGYQQGRYGPYNSNY-----  
87 -----MKKFFSQSLLAL-IISMNAVSGMDG--NGVFLGAGYLOGQAQMHADIN-----  
116 -----MKKFFSQSLLAL-IISMNAVSGMDG--NGVFLGAGYLOGQAQMHADIN-----  
84 -----MARULMKKFVALGLLSAVLSSSLAEGDGVYIGTNYQLGQARLNSNIYNTGDCTGS  
                  \* . . . \*                   \* . . . . \* \*

74 -----SDWRHGN-DLYGLNFKLGFGVFAN-----BLOCK B  
115 -----SDWRHGN-DLYGLNFKLGFGVFAN-----BLOCK C  
87 -----SQKQATNATIKGFDALLGYQFFFE-----KWFGARV  
116 -----SQKQATNATIKGFDALLGYQFFFE-----KHFGRL  
84 VVGCPPLTANKHNPGGTNINWHSKYANGALNGFGLNVGYKKFFQFKSLDMTSKWFGFRV  
                                  \* . . \*                   \* . . . \*

74 YGFLDWFNTSGTEHT-----KTNLLTYGGGGD  
115 YGFLDWFNTSGTEHT-----KTNLLTYGGGGD  
87 YGFFDYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD  
116 YGFFDYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD  
84 YGLFDYGHADLGKQVY-----APNKIQLDMSVSWGVGSD  
\*\* \*                   . . . \* \*

74 LIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQ-----BLOCK D  
115 LIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQ-----  
87 VMVNVINNGIMSLGAFGGIQLAGNSWLMATPSFEGILVEQAL-----V  
116 VMVNVINNGIMSLGAFGGIQLAGNSWLMATPSFEGILVEQAL-----V  
84 LLADIIDKDNASEGIFGGVAIGGNTWKSSAANYWKEQIIEAKGPDVCTPTYCNPAPYST  
.. . \*                   \* . . . . \*

74 -----TRFQFLWNLGGRMRVGDRSAFEAGVKFPMVNOG-----BLOCK E  
115 -----TRFQFLWNLGGRMRVGDRSAFEAGVKFPMVNOG-----BLOCK F  
87 SKKATSFQFLFNVGARLRILKHSSIEAGVKFPMLEKKNPYIT---AKNLDIGFRRVYSWYV  
116 SKKATSFQFLFNVGARLRILKHSSIEAGVKFPMLEKKNPYIT---AKNLDIGFRRVYSWYV  
84 NTSTVAFQVWLNFGVRANIYKHNGVEFGVRVPLLINKFLSAGPNATNLYYHLKRDYSLYL  
\*\* \* . . . . \* . . . . \*

74 DYVFTF  
115 DYVFTF  
87 NYVFTF  
116 NYVFTF  
84 GYNYTF  
\* . . \*

FIGURE 5

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aaSeqID#
83      MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
89      -----
108     MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
118     MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
*****

83      ILKRAANLFTNAEAI SKLKFSSLS PVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
89      -----
108     ILKRAANLFTNAEAI SKLKFSSLS PVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
118     ILKRAANLFTNAEAI SKLKFSSLS PVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
*****

83      IDLGV IETIPKHSKIVLPGEAFDSL-----KIDPYTLFLPKIEATSTSISDANTQRVFET
89      ----VIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTFFFPKFEATSTSISDINTQRVFET
108     IDLGV IETIPKHSKIVLPGEAFDSLKEAFDKIDPYTLFLPKFEATSTSISDINTQRVFET
118     IDLGV IETIPKHSKIVLPGEAFDSL-----KIDPYTLFLPKIEATSTSISDANTQRVFET
*****

83      LNKIKTNLVVNYRNEN-----KFKDHENHWEAFTPQTAEFTNLMLNMI AVLDS
89      LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDWCQNFTPQTAEFTNLMLNMI AVLDS
108     LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDWCQNFTPQTAEFTNLMLNMI AVLDS
118     LNKIKTNLVVNYRNEN-----KFKDHENHWEAFTPQTAEFTNLMLNMI AVLDS
*****

83      QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
89      QSWGDAILNAPFEFTNSSTD CSDSPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
108     QSWGDAILNAPFEFTNSSTD CSDSPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
118     QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
*****

83      DLDVIVLKDSGVVGLGSDITPSNNDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
89      EIDAVVLKNSGVVGLANGY-----NDG-EYGT LGVEAYALDPKKLFGDNLKTINLEDLRT
108     EIDAVVLKNSGVVGLANGY-----NDG-EYGT LGVEAYALDPKKLFGDNLKTINLEDLRT
118     DLDVIVLKDSGVVGLGSDITPSNNDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
*****

83      ILHEFSHTKGYGHNGNMTYQRPVPTKDGQVEKDSNGKPKDS DGLPYNVC-----
89      ILHEFSHTKGYGHNGNMTYQRPVPTKDGQVEKDSNGKPKDS DGLPYNVC SLYGGSNQPAF
108     ILHEFSHTKGYGHNGNMTYQRPVPTKDGQVEKDSNGKPKDS DGLPYNVC SLYGGSNQPAF
118     ILHEFSHTKGYGHNGNMTYQRPVPTKDGQVEKDSNGKPKDS DGLPYNVC SLYGGSNQPAF
*****

83      -----
89      PSNYPNSIYHNCADV PAGFLGVTA AVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL
108     PSNYPNSIYHNCADV PAGFLGVTA AVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL
118     PSNYPNSIYHNCADV PAGFLGVTA AVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL
*****

```

FIGURE 6

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83  
89  
108  
118  
-----  
ANSMLSTIQKTFVTSSVTNNHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY  
ANSMLSTIQKTFVTSSVTNNHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY  
ANSMLSTIQKTFVTSSVTNNHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY  
\*\*\*\*\*  
-----  
83  
89  
108  
118  
-----  
NYAKAVNQKVQQLSYGGIDLLDFITTSNKNSPGTGIQTKRNFSSSFGIFGGLRGLYNS  
NYAKAVNQKVQQLSYGGIDLLDFITTSNKNSPGTGIQTKRNFSSSFGIFGGLRGLYNS  
NYAKAVNQKVQQLSYGGIDLLDFITTSNKNSPGTGIQTKRNFSSSFGIFGGLRGLYNS  
\*\*\*\*\*  
-----  
83  
89  
108  
118  
-----  
YYVLNKKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVSSGGDYTNSFVFNEGA  
YYVLNKKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVSSGGDYTNSFVFNEGA  
YYVLNKKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVSSGGDYTNSFVFNEGA  
\*\*\*\*\*  
-----  
83  
89  
108  
118  
-----  
SHFKVFFNYGGCF  
SHFKVFFNYGWVF  
SHFKVFFNYGWVF  
\*\*\*\*\*

FIGURE 6 (Cont'd)

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aaSeqID

80  
112

VLKFQKLPLL FVSILYNQSPLLAFDYKFSGVAESVSKVGFNHSKLN SKEGIFPTATFVTA  
-----VSYDN-----TDDYYFP-----RNGVIFSSYATMSGLPSSGTLNSW  
\* \* \* \* \*

BLOCK A

80  
112

TIKLQVDSNLLPKNIEKHSKIGVGGILGALAYDSTKTLIDQATHQIYGSELFYLIGRWW  
N-----G-----LGGNVRNTKVYGKEAYHHLQKYLIDLIARFK  
\* \*\*  
\* \* \* \*

BLOCK B

80  
112

GFLGNAPWKDSLIESDAHTRNYVLNSYLFYSYGDKFHLKLG RYLSNMDFMSSYTQGFEL  
TQGG-----YIFR-----YNTDDYLPLNSTFYMGGVTTVRGFRNG-----  
\* \* \* \* \*

80  
112

DYKINSKIALKWFSSFGRALAFGQWIRDWYAPIVTE DGRKEVYDGIHAAQLYFSSKHVQV  
-----SITPKDEFGLWLG-----G-----DGIFTASTELS  
\* \* \* \* \*

BLOCK C

80  
112

MPFAYFSPKIYGAPGVKIHIDSNPKFKGLGLRAQT TINVIFPVYAKDLYDVYWRNSKIGE  
-----YG-----VLKAAKMRLAWFFDFGFLT FKTPTRG SFFYN-----  
\* \* \* \* \*

BLOCK D

80  
112

WGASLLIHQRFDYNEFNFGFGYYQNF GNANARIGWYGNPIPFNYRNNSVYGGVFSNAITA  
--APTTTANFHDYGVVGAGFERATWRASTGLQIEWISPMGPLVL-----  
\* \* \* \* \*

80  
112

DAVSGYVFGGGVYRGFLWGILGRYTYATRASERSINLNLGYKWGSFARVDVNLEYVYVSM  
-----IFPIAFFN-----QWG-----D  
\* \* \*

BLOCK E

80  
112

HNGYRLDYLTGPFNKAFKADAQDRSNLMVSMKFFF  
GNGKKCKGLC--FNPNMNDYTQ--HFEFSMGTRF  
\* \* \* \* \*

FIGURE 7

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## FIGURE 8

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/19575

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A01N 43/04; A61K 31/70; C12Q 1/68

US CL : 514/44; 435/6

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/44; 435/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
GENEBANKElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
NONE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TAYLOR, et al. Construction of a <i>Helicobacter pylori</i> Genome Map and Demonstration of Diversity at the Genome Level. Journal of Bacteriology. November 1992, Vol. 174, No. 21, pages 6800-6806, see entire document.	1-65
A	AKOPYANZ, et al. DNA diversity among clinical isolates of <i>Helicobacter pylori</i> detected by PCR-based RAPD fingerprinting. Nucleic Acids Research. 1992, Vol. 20, No. 19, pages 5137-5142, see entire document.	1-65



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*&* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

27 FEBRUARY 1998

Date of mailing of the international search report

13 MAR 1998

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

GINNY PORTNER

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/19575**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  
1-65, SEQ. ID Nos. 1, 7, 8, 11, 37, 39, 43, 45, 55, 61, 74, 80, 81 and 112
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☒

No protest accompanied the payment of additional search fees.



## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/19575

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-26, 47, 49, 51, 53, 55, 57, 59, and 61, drawn to no fewer than 135 nucleic acid molecules, vectors containing the nucleic acid molecules, DNA encoding fragments of the polypeptides encoded by the no fewer than 135 different DNAs, organism transformed with the nucleic acid molecules, vaccines and methods of producing polypeptides encoded by the no fewer than 135 different nucleic acid molecules.

Group II, claim(s) 27-46, 48, 50, 52, 54, 56, 58, 60, and 62-65 are, drawn to no fewer than 73 polypeptides encoded by a subset of the encoding DNA mentioned in Group I.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I contains a separate DNA species for each sequence mentioned. Therefore, there is a minimum of 135 species.

Group II contains at least one polypeptide for each DNA sequence mentioned. Therefore, this is a minimum of 73 species in Group II.

For either Group that applicant elects, a total of 10 (ten) specified sequences will be searched and no more than 4 (four) specified sequences will be searched for each additional fee paid; if no additional fee is paid and no election indicated the first 10 sequences appearing in Group I will be searched.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The polypeptide encoding DNAs, vectors containing them, organisms transformed with them and methods of polypeptide production using them of Group I are materially different from each other and are therefore independent from the polypeptides of Group II. Additionally, none of the products or methods of Group I is needed to make the polypeptides of Group II.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: There is no relationship between or among the various nucleotide and amino acid sequences mentioned in the claims.

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